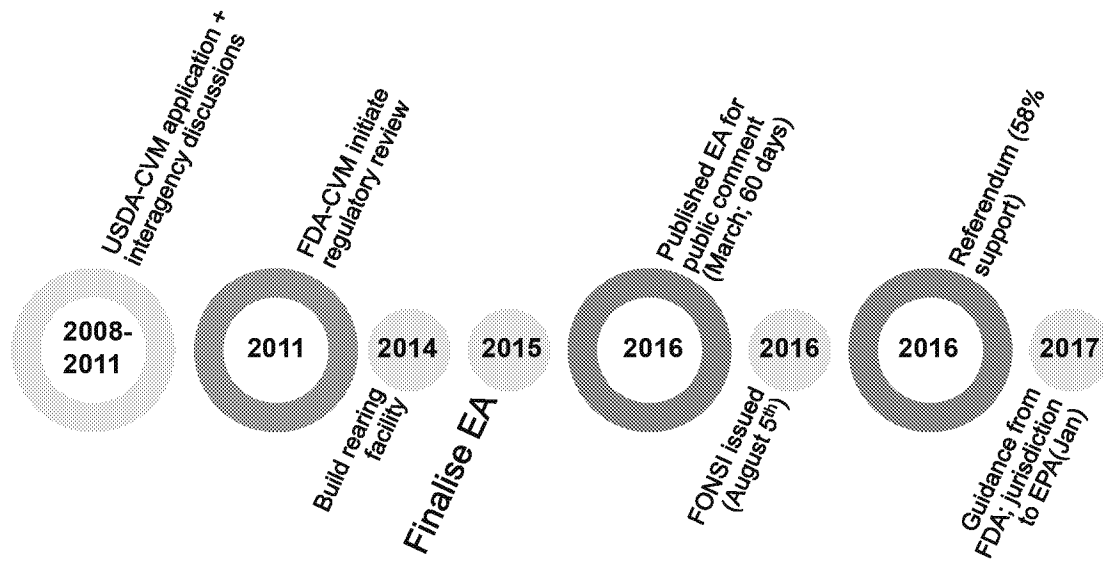


Regulatory Status of OX513A



Regulatory History in the US



Regulatory History (Annotated)






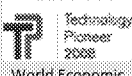




| Date | Agency | Outcome |
|---------------------|--|---|
| Apr 2008 – Nov 2011 | Interagency discussions re for GE mosquito field trial <ul style="list-style-type: none"> USDA-APHIS-BRS EPA CDC USDA-APHIS-PPD USDA-APHIS-VS | Oct 2009 – USDA-VS-NCIE has jurisdiction Mar 2010 – Application for trial submitted to USDA-VS-NCIE NOV 2011 – USDA-VS-NCIE issues letter of no jurisdiction Nov 11 – FDA-CVM has jurisdiction 3 YEARS to determine which agency has jurisdiction |
| 23 Nov 2011 | Oxitec opened INAD file 012-109 with FDA | 2011 – 2016: requested further information. Achieved concurrence re sections of file (e.g., Molecular characterisation, GE animal lineage, trial protocol) |
| 11 Mar 2016 | FDA_CVM post Oxitec's draft EA and FDA's preliminary FONSI for public comment | |
| 5 Aug 2016 | FDA – CVM FINAL FONSI Key Haven published | Approx. 5 years to achieve a final FONSI for one trial site |
| 28 Oct 2016 | INAD file 012-109 – resubmitted for a new trial site in Monroe County | Amendment submission sent 4 Nov 2016 |
| 14 Dec 2016 | FDA's letter re incomplete EA | |
| Jan 2017 | FDA_CVM release for comments - Draft Guidance for Industry #236 – Regulation of mosquito related products. Allows jurisdiction transfer to EPA. | Deadline for comments Feb 21 2017 |
| Mar 2017 | INAD file 012-109 – re submitted with expanded draft EA for trials and endangered analysis (ESA) resubmitted | |
| 28 Apr 2017 | FDA -CVM request further clarifications/ information re trial sites and ESA | |

Oxitec Historical Overview



OXITEC

| |  Pink bollworm | |  OX513A | |  Brazil facility | |  OX513A Emerging |
|---|--|---|--|---|--|--|--|
| 2002/4 | 2005/7 | 2008/9 | 2010/12 | 2013 | 2014 | 2015 | 2016/17 |
| <p>Company formed as spin out from Oxford University</p> <p>Technology platform developed and exemplified in both agricultural and mosquito species</p>  <p>Injection of DNA</p> | <p>Global first release of a GE insect Pink Bollworm (marker only) in USA</p> <p>Mosquito development spurred by Gates funding</p> | <p>First outdoor release of OX513A mosquito in the Caymans</p> <p>Environmental Impact Statement in the USA (GE Pink Bollworm) – environmentally preferred solution</p>  <p>Technology Pioneer 2008 World Economic Forum</p> | <p>First outdoor release of OX513A in Brazil</p> <p>First agricultural collaborations</p> <p>Oxitec Brazil established</p> | <p>Outdoor trials of OX513A in Panama and Brazil</p> <p>First larger scale urban project starts in Jacobina, Brazil</p> <p>First agricultural strains into development Medfly, DBM & Olive fly</p>  <p>Oxitec medfly</p> | <p>Oxitec Brazil National Biosafety approval in Brazil</p> <p>Panama outdoor trial</p> <p>Brazil approval for agricultural trial</p> | <p>First independent projects of OX513A Brazil</p> <p>Oxitec acquired by Intrexon to accelerate development</p>  <p>New UK facility</p> | <p>WHO issues recommendation for OX513A</p> <p>ANVISA announces it will issue RET</p> <p>Grand Cayman launches OX513A</p> <p>FDA publishes final FONSI & EA for Florida Keys</p> <p>Monroe County vote 58% in favour of OX513A</p> <p>Piracicaba expands project & opens new production facility</p> <p>OX513A project begins in India</p> |

Step-Wise Evaluation – Field Release OXITEC

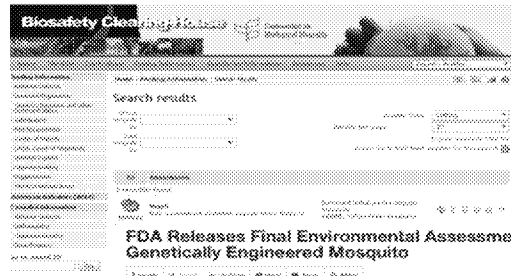
| Cayman | Malaysia | Cayman | Brazil | Brazil | Panama | Brazil | Brazil | Brazil | Cayman |
|----------------------------------|------------------|--------------|--------------|--------------|-----------------|--------------|------------------|--------------------|------------|
| East End | Bentong | East End | Itaberaba | Mandacaru | Nuevo Chorillio | Jacobina | Piracicaba CECAP | Piracicaba CENTRAL | West Bay |
| 2009 | 2010 | 2010 | 2011-12 | 2012-13 | 2014 | 2013-14 | 2015→ | 2016→ | 2016→ |
| 1 st open release MRR | Open release MRR | >90% control | >90% control | >90% control | >90% control | >90% control | (On-going) | (On-going) | (On-going) |
| NA | NA | 2-300 | 1,800 | 2,800 | 1,000 | 1,500 | 5,000 | 65,000 | 2 → 50,000 |

Initial proof concept, behavioural studies

Operational optimization/use

- Dispersal - > release pattern required
- Longevity - > release interval required
- Monitoring systems
- Dose/release rate required
- Build regulatory dossier
- Release optimization
 - Spatially and temporarily
 - Adaptive release rate
- Monitoring systems optimization
- Mass rearing and Distribution chain
- Data Management System

Approvals in Multiple Countries



FDA Releases Final Environmental Assessment for Genetically Engineered Mosquito

August 16, 2016

The FDA has completed the environmental review for a proposed pilot study to determine whether the release of OXITEC's genetically engineered (GE) mosquitoes (GEMs) will suppress the local vector mosquito population in the release area of Fort Lauderdale, Florida. After considering thousands of public comments, the FDA has published a final environmental assessment (FEA) and finding of no significant impact (FONSI). The FEA and FONSI are available at <https://www.fda.gov/oc/ohrt/oxitec-gem-fda-fon-si>.

Mosquito (vector) control emergency response and preparedness for Zika virus

10 March 2015 | 11:00am

Summary

On 14-16 March 2015 the 66th Vector Control Advisory Group (VCAG) reviewed the proposed vector control trials and existing trials for Zika in the context of the response to the Zika virus outbreak. The agenda included: (1) mosquito control of human mosquitoes in adult vectors (Othello); (2) mosquito control through genetic manipulation (GEMs); (3) vector control through (4) vector traps; and (5) mosquito control through (6) vector traps.

The main conclusions and recommendations of the meeting are as follows:

- 1. The 66th VCAG recommended vector control programmes using existing tools and strategies for efforts to reducing the transmission of Zika virus, including the use of GEMs. These efforts should be coordinated and used to control the Zika virus. They include: (a) targeted mosquito spraying; (b) vector control; (c) vector control; and (d) vector control.
- 2. The 66th VCAG recommended that the release of GEMs be delayed until the release of the first and second trials reviewed by VCAG. However, the 66th VCAG recommended the specific release of GEMs under operational conditions of the first trial (Othello) and second trial (Othello) to be delayed until the release of the first and second trials reviewed by VCAG.
- 3. The 66th VCAG concluded that more evidence is required before consideration of the pilot deployment of the first additional trials reviewed by VCAG. These trials include: (a) vector traps and (b) vector traps.

April 2014

March 2016

April 2016

July 2016

July 2016

August 2016

November 2016

Brazil's CTNBio granted approval for commercial release of Friendly™ Aedes

World Health Organization issued recommendation for pilot deployment of Friendly™ Aedes

ANVISA announced will issue RET (special temporary registration)

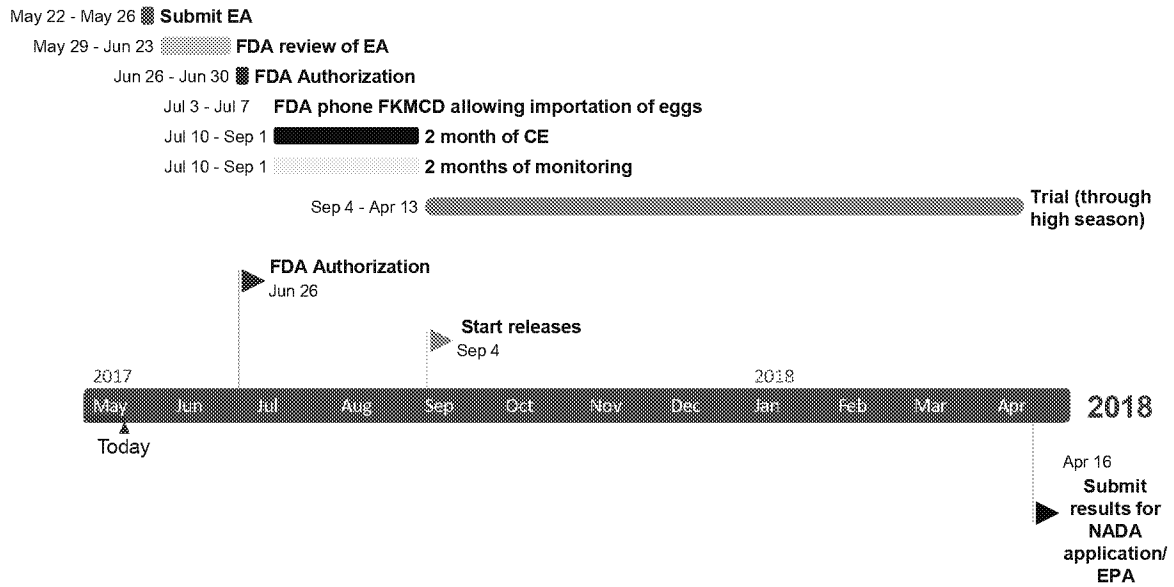
Piracicaba, Brazil, started release of Friendly™ Aedes for expansion to cover 60K people

Grand Cayman launched Friendly™ Aedes to suppress wild Aedes aegypti

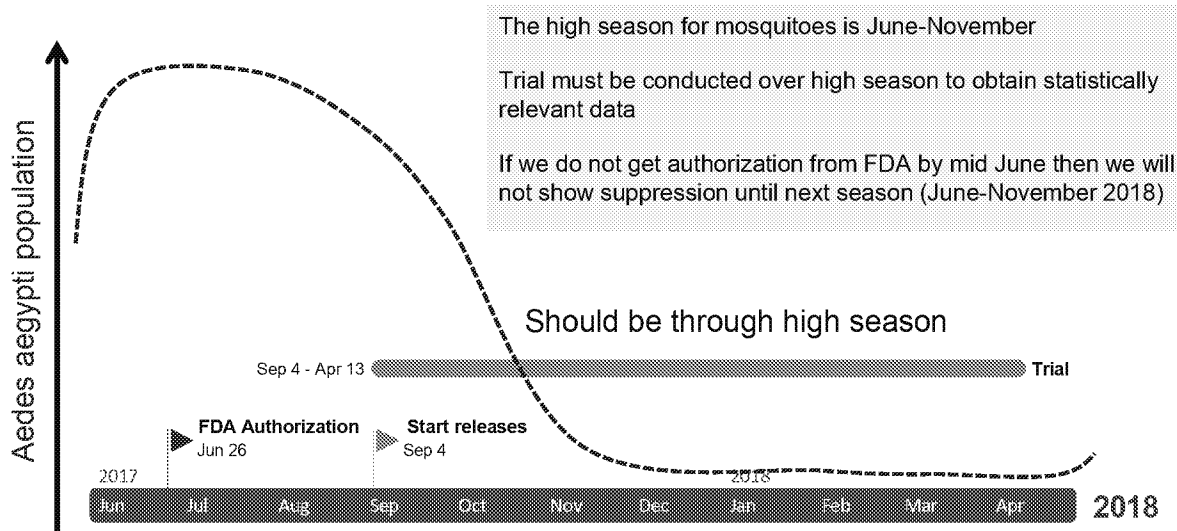
FDA published final FONSI and environmental assessment for trial in Florida Keys

Florida Keys Mosquito Control District voted to approve trial of Friendly™ Aedes

Timeline for Monroe County Trial



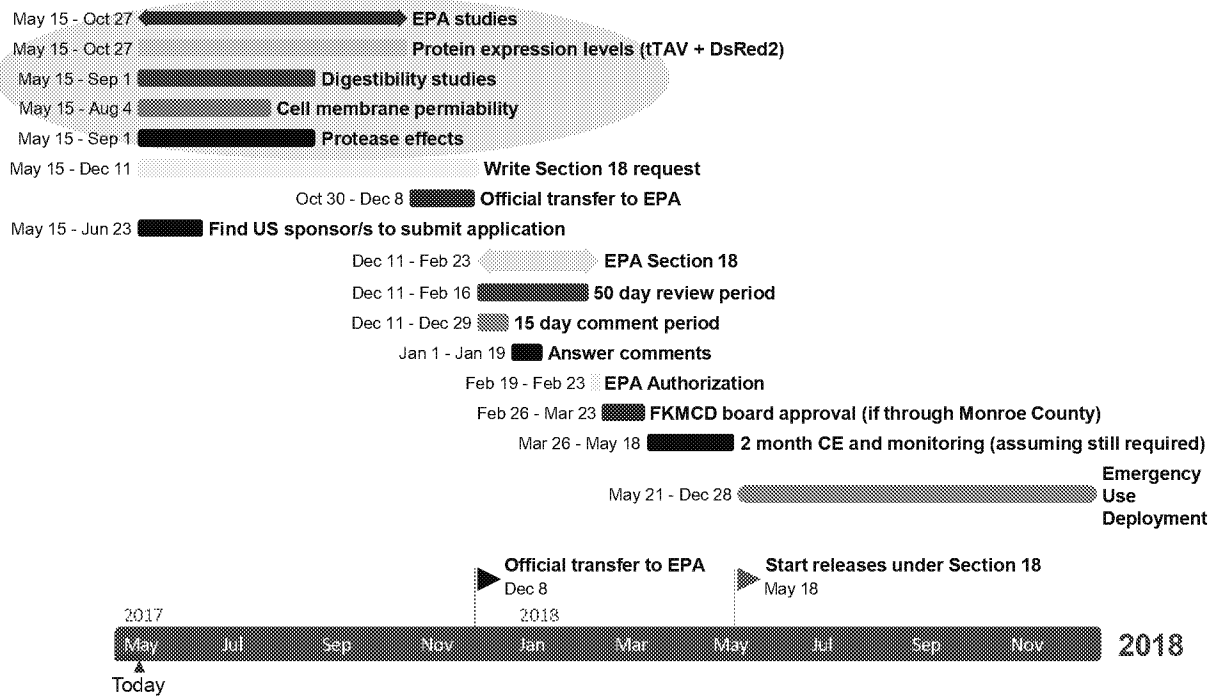
Seasonality of *Aedes aegypti*



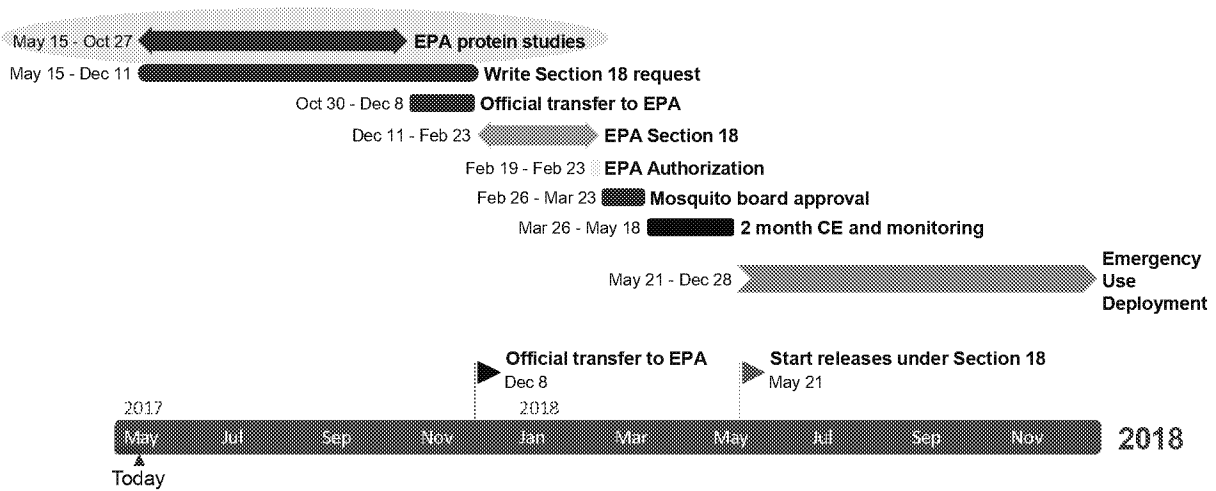
Timeline for Section 18 EPA/FDACS



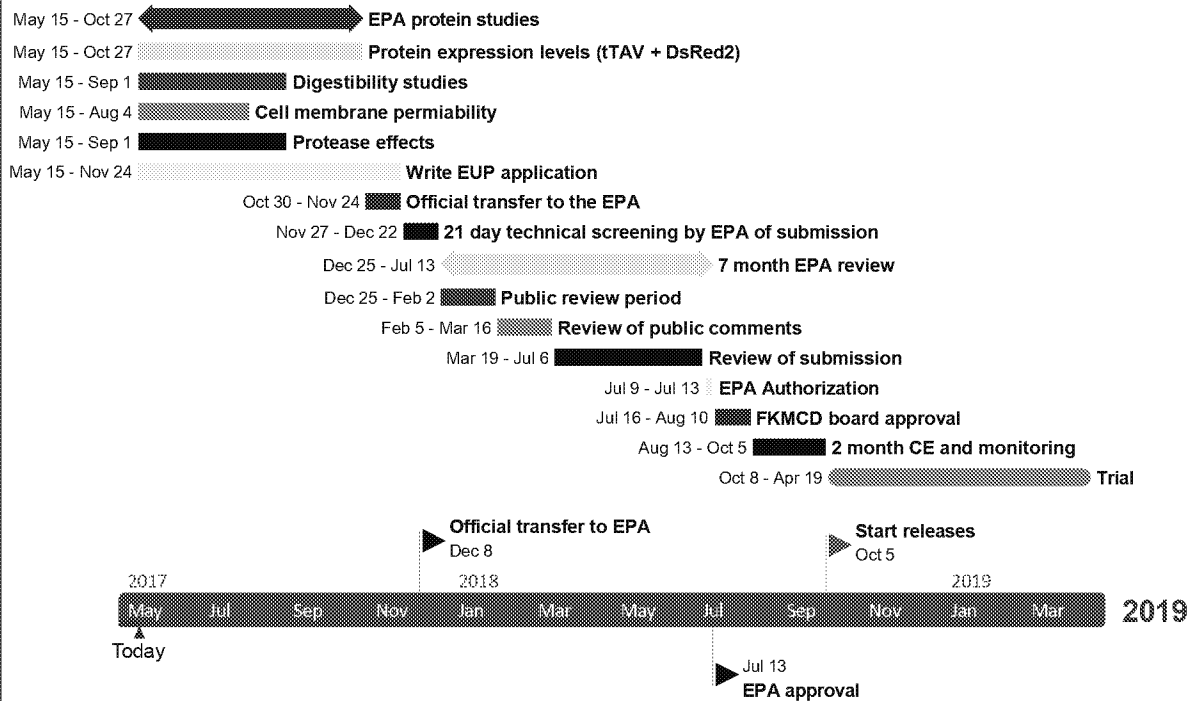
OXITEC



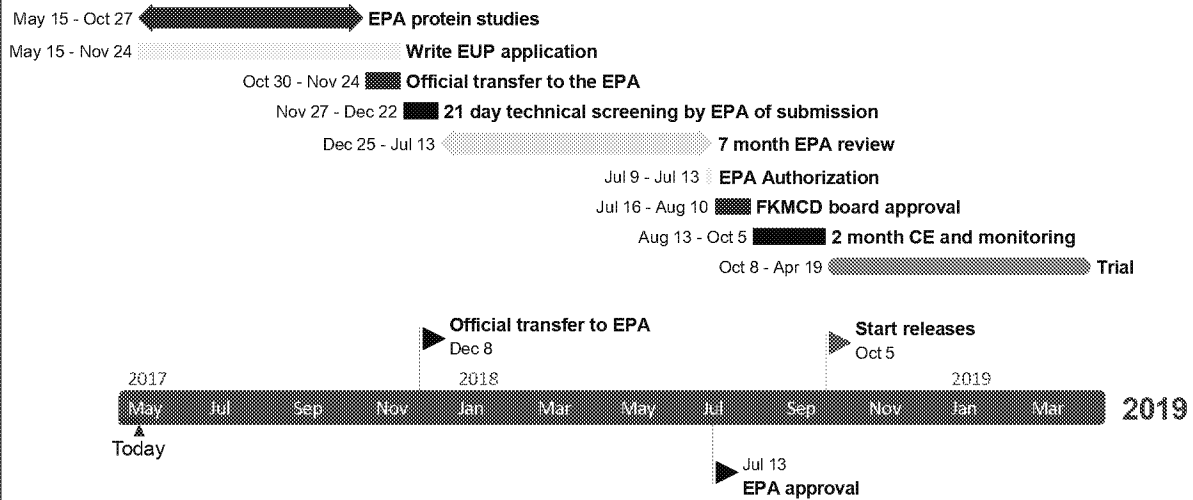
Estimated Timelines for Emergency Use Approval



Timeline EPA EUP Route (Full)



Estimated Timelines for Experimental Use Permit



Section 3 Registration



Estimated Timeline for Section 3 Registration

